Claims 112, 114-126, 131, 133, 135-157, 159, 161-172, 176, 178 and 189-196 stand rejected. Claims 158, 160, 173-175, and 179-188 have been objected to.

Claims 112-134, 137, 139-141, 146, 152-155, 164, 170, 171, 177, 182, 183, 191, 195 and 196 (a total of 43 claims) have been cancelled without prejudice. In addition, new claims 197-212 (a total of 16 claims) have been added.

In accordance with the Examiner's request, Applicants have attached hereto a clean copy of the pending claims. A detailed description of the amendments is also attached to this paper.

In addition, Applicants note that the Office Action, on the summary page thereof, has been checked as both a Final Action and a Non-Final Action. Applicants' agent contacted the Examiner and was informed that the check mark indicating "Final Action" was in error and that this Office Action is Non-final.

Drawings

The Examiner has maintained the objection to the drawings and Applicant has submitted herewith, along with a Letter to the Official Draftsperson, a copy of formal drawings for the present application. No new matter has been added. However, because of constraints of point size and margins, some of the figures have been extended over to additional sheets. Thus, 76 sheets of drawings have been submitted in place of the 68 sheets originally filed. The particulars of these changes are described in more detail in the Letter to the Official Draftsperson that accompanies the formal drawing sheets. The objection noted by the Examiner in the Office Action of 19 June 2001, regarding Figure 12, has been corrected. Applicants will await the Official Draftperson's review. No amendment to the specification or drawing descriptions has been made.

Claim Objections

Claims 174, 175, 179-188 have been objected to as containing an improper multiple dependency. In response, Applicants have cancelled claims 182 and 183 and have amended the remaining claims to remove any improper multiple dependency.

In addition, claims 179, 181, 182, 184, 187 and 189 have been amended to clarify that there are no multiple dependencies.

Claims 158, 160, 173, 179, 181, 182, 184 and 187 were objected to on grounds that they do not refer back in the alternative. In response, claim 182 has been cancelled and the remaining claims amended to recite single claim dependency.

Claims 112, 135, and 139 have been objected to for use of the phrase "a ABC1" instead of "an ABC1." In response, claims 112 and 139 have been cancelled and claim 135 amended to recite "an" in place of "a" at the required location.

Claim 146 was objected to for use of abbreviations. In response, this claim has been cancelled.

Claim 165 was objected to as being of improper dependent form. In response, this claim has been amended to depend from claim 161 instead of claim 160, in accordance with the Examiner's suggestion.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 114, 162-164, 176 and 191 have been rejected under section 112 as being indefinite.

In response, claim 114 has been cancelled.

Claims 162-164 have been rejected for apparent improper claim dependency. In response, these claims have been amended to depend from claim 161 instead of claim 160, in accordance with the Examiner's suggestion.

Claim 176 was rejected as indefinite for recitation of the term "hABC1," which would imply wild-type protein and not mutant protein. In response, claim 176 has been amended to recite a mutant ABC1.

Claim 191 was rejected for implying that a cell that expresses ABC1 would have no expression when the test compound is not present. In response, claim 191 has been cancelled.

Rejection Under 35 U.S.C. §112, First Paragraph (Written Description)

Claims 112, 114-126, 131, 133, 135-157, 159, 161-172, 176, 178, and 189-196 were rejected as failing to meet the written description requirement on grounds that the claims are overly broad.

The Office Action makes reference to a previous rejection of the claims on this ground, although a new claim set has been added since, with some claims further amended by a Supplemental Amendment. In response, applicants note that the new claims represent a clearer description of the invention. The previous office action had stated that the specification disclosed the structure of only the human ABC1 but Applicants note that the structure for mouse ABC1 is also disclosed, as was pointed out

in Applicants' previous response. The previous rejection under the written description requirement was predicated on the argument that Applicants' claims were too broadly stated and that the specification failed to describe any other representative species by identifying characteristics or properties other than the functionality of being an ABC1 polypeptide.

In response, Applicants have cancelled claims 112, 114-126, 131, 133. In addition, claims 139 – 141, 146, 152-155, 170, 171, 191, and 195 have also been cancelled.

Of the generic claims, claim 135 has been amended to recite use of a human ABC1 as modulating either ATP binding or ATP hydrolysis.

Claim 143, directed to an assay involving lipid transport, has not been limited to mouse and human for the following reason. ABC1 protein is ATP-binding cassette transporter protein (which, as the Examiner knows, is the meaning of "ABC") and thus such polypeptides, regardless of the source, are expected to have similar properties (i.e., ATP-binding cassette transporter properties). Applicants note that the claims are directed to methods of identifying ABC1 modulating agents using assays of ABC1 biological activity and such activities would be expected to be similar from one animal to another because that is what makes them ABC1 polypeptides. In the present case, Applicants have discovered a new ABC1 activity, viz., lipid transport activity, such as the transport of cholesterol, and have developed a lipid transport assay based on this process, which is a physiological process.

Thus, claim 143 is directed to use of Applicants' assay methods (for example, the cholesterol efflux assay disclosed on page 72 of the application as filed) with and without the presence of a modulating agent. The purpose of the assay is to test for modulation so that providing a function and an assay procedure to measure that function is sufficient to show that Applicants are in possession of the claimed method,

especially since no one else knew of this function prior to Applicants' teaching. As to the variety of the polypeptides to be screened (here, mammalian ABC1 polypeptides), Applicants note that functionality is all that is required to apply the method. The sequences of the various ABC1 proteins are not required. In fact, the Luciani et al reference, at page 229, column 2, bottom, indicates that ABC1 is highly conserved across evolution.

Reliance on the decision in *U. Calif. v. Eli Lilly* is misplaced. In *Eli Lilly* the claim being sought was directed to polypeptides of species other than those disclosed in the application. That is far different from the claims of the present application. The court in *Eli Lilly* was talking about claims directed to genetic material, which is expected to vary in sequence, there "mammalian insulin cDNA" and, where the claim is to the cDNA itself, expected variations in sequence among different species would certainly tell those skilled in the art that the inventors were not in possession of the polypeptide sequences of other species at the time their application was filed. In short, the claims in *Eli Lilly* were directed to polypeptides of different species merely because they had the sequence one of them. However, while claims to different insulin polypeptides would not be supported by merely disclosing a polypeptide from one species, those skilled in the art would not argue that insulin proteins, regardless of the species, play a role in regulating blood sugar metabolism (since that is what insulin does) and thus an assay for insulin activity would be supported regardless of source.

In the present application, Applicants' claims rely on an assay of functionality of an ABC1 polypeptide. In addition, Applicants teach a physiological function for the ABC1 polypeptide (the rejection concedes that such a function was not known at the time of filing (see Office Action at page 9, lines 16-18)). Thus, Applicants teach that mutations in specific regions are intimately associated with defects in lipid metabolism. For example, the results referred to in the application at page 28, lines 9-11, show that the individuals whose lineage is depicted in Figure 1C had Tangier's Disease (thus, low HDL and consequent elevated cholesterol levels). This is further supported by the

results described at page 38, lines 7-21, of the application where correlation between lipid metabolism and ABC1 mRNA production was shown.

Thus, the claims being examined are not directed to ABC1 polypeptides of different species but rather are directed to assays (i.e., functionality) of these polypeptides in identifying modulating agents. Thus, in using the methods of the invention, one does not need to know specifically the structure of the polypeptide ahead of time and the structure may not actually be known. Thus, at page 62, lines 7-11, the effects on lipid metabolism are noted for a number of different species.

For example, if one were isolating the ABC1 protein from a new source (for example, sheep), one could use the cholesterol efflux assay to follow the specific activity of the purified fractions through each step of purification, and thereby obtain a purified ABC1 product (and secure a patent claim to a highly purified ABC1 without knowing the amino acid sequence). Applicants, based on the teaching of the application, are certainly in possession of a novel and sensitive physiologically relevant assay for ABC1. This is even more so in light of the fact that because Applicants teach the first physiological function for ABC1, no others in the art would have any motivation to identify modulators of ABC1 proteins for clinical or other uses.

In sum, because functionality is the underlying property of ABC1 polypeptides to be used in the methods of the invention, Applicants have fully enabled claims to using such function to identify modulators of ABC1 biological activity by enabling such assays with human and mouse proteins and without having to disclose the amino acid sequence of all mammalian ABC1 proteins, or even a substantial number of them.

Furthermore, Applicants show that such function is likely to be conserved across different species. For example, Applicants show that the sequence of the mouse ABC1 is highly homologous to that of the human, the correct sequence of which was unknown

prior to the present application and the physiological function of the mouse protein was likewise not known prior to the present invention.

Specific polymorphisms or mutations in ABC1 are described in the application beginning at page 81. Also, Figure 4B shows the sequence homology for species as diverse as human, mouse, CAEEL (C. elegans) in a region of the gene where the mutation in the patient (nucleotide 4503) plays a role in lipid metabolism defects. The same can be said for the region of the gene and protein depicted in Figure 5B. A similar result holds for the region depicted in Figure 6B. Further, Figure 15 shows homology in a sequence from mouse, human and chicken. These regions of the ABC1 genes and proteins from these different species represent regions intimately associated with lipid metabolism, especially the lipid transport, including cholesterol efflux, function of the protein. Because these critical regions are conserved across diverse species, and these regions have been shown by Applicants to be important in the physiological functioning of ABC1 in humans, those skilled in the art would certainly be justified in expecting that a similar physiological function would be found in ABC1 proteins from different species, especially from different mammals as recited in claim 143. In addition, Applicants have added new claims 209 (WHAM chicken) and 210 (C. elegans). In fact, the Luciani and Chimini reference relied on in the rejection on 102/103 grounds (see below) attests to the fact that ABC1 is highly conserved across evolution.

Claim 161, and all claims dependent therefrom, has been amended to recite use of a human ABC1 protein that comprises amino acid residues 1-60 of SEQ ID NO: 1, the latter sequence not being known prior to Applicants' teaching herein.

Claim 166, and all claims dependent therefrom, has been amended to recite use of a human ABC1 protein wherein the compounds are for use in treating a coronary artery disease (CAD), a problem observed at high frequency in those suffering from Tangier's disease (mentioned above). The relevance of ABC1 in disease was not known

prior to Applicants' teaching herein and so Applicants are certainly in possession of the clinical relevance of ABC1 activity based on the Application as filed.

Claim 169, and all claims dependent therefrom, has been amended to recite use of a human ABC1 protein that comprises amino acid residues 1-60 of SEQ ID NO: 1, the latter sequence not being known prior to Applicants' teaching.

Claim 189, and all claims dependent therefrom, has been amended to recite use of a genetic construct comprising an ABC1 promoter, such as that disclosed in Figure 3 (BAC RPCI-11 317 for human ABC1), operably linked to a reporter gene, as supported in the application, especially at page 8, lines 17-28, in combination with the genomic structure shown in Figure 3.

Rejection Under 35 U.S.C. §112, First Paragraph (Scope of Enablement)

Claims 112, 117, 118, 122, 123, 131, 133, 135, 137-139, 141-144, 155, 157-161, 164, 166-171, 176, 178 and 189 have been rejected on grounds that they are not fully enabled by the specification as filed. Applicants believe that this is basically a continuation of the rejection for failure to meet the written description requirement and therefore initially reasserts all of the foregoing arguments related to establishing the written description of the invention in light of the amendments made in the present response.

In response, Applicants have cancelled claims 112, 117, 118, 122, 123, 131, 133, 139, 141, 155, 170 and 171.

The rejection urges that the specification is not enabling for a process to identify a compound that modulates any mammalian ABC1 polypeptide using any lipid that is

any part of HDL-cholesterol or any fragment of HDL-cholesterol. In response, Applicants have amended claim 143, and claims dependent therefrom, to recite use of phospholipid or cholesterol with either mouse or human ABC1. This is fully enabled throughout the application for the reasons already discussed regarding written description.

The rejection also urges that the specification is not enabling for a process to identify a compound that modulates any mammalian ABC1 polypeptide by detecting a difference in ATP hydrolysis. Applicants have amended claim 135 to recite use of human ABC1 protein with the ATP hydrolysis or binding assays. In addition, dependent claims 138 and 142 have been amended to recite use of proteins having specified sequences for the human ABC1. These claims are fully enabled in the application.

The rejection further urges that the specification is not enabling for a process to identify a compound that modulates any mammalian ABC1 polypeptide by detecting a difference in lipid transport using any acceptor that accepts a transported lipid and where the lipid can be any part or fragment of HDL cholesterol. Applicants respond that the acceptor is one of phospholipid, HDL cholesterol or ApoAI, ApoA2 and ApoE. Claim 144 has been amended to recite this limitation while claim 145 has been amended to recite that the compound is useful in treating coronary artery disease (CAD), claim 146 has been cancelled and claim 147 amended to recite that the cholesterol is part of HDL-cholesterol.

The rejection also argues that the specification is not enabling for a process to identify a compound that modulates any mammalian ABC1 polypeptide in a membrane by detecting a difference in ion transport in the presence or absence of a test compound. In response, Applicants have amended claim 161, and claims dependent therefrom, to recite use of a human ABC1 protein comprising amino acid residues 1-60 of SEQ ID NO: 1.

Claim 166, and claims dependent therefrom, directed to use of an assay involving interleukin binding, has been amended to require that the compound be compound found to be a modulating agent be useful in treating a coronary artery disease. This is fully enabled because Applicants for the first time show the involvement of ABC1 in the presence of coronary artery disease within human families.

The rejection also contends that the specification is not enabling for a process to identify a compound that modulates any mammalian ABC1 polypeptide by detecting a difference in binding to a protein in the presence or absence of a test compound. In response, Applicants have amended claim 169, and claims dependent therefrom, to recite use of a human ABC1 protein comprising amino acid residues 1-60 of SEQ ID NO: 1.

The rejection further contends that the specification is not enabling for a process to identify a compound that modulates any mutant mammalian ABC1 polypeptide by detecting a difference in binding to a lipid, a protein, ATP, and interleukin-1 in the presence or absence of a test compound. In response, Applicants have amended claim 176 and 178 to reflect that only a mutant human ABC1 protein is used.

The rejection then argues that the specification is not enabling for a process to identify a compound that modulates any ABC1 polypeptide expressed in a cell by detecting a difference in ABC expression in the presence or absence of a test compound. In response, claim 189, and all claims dependent therefrom, has been amended to recite use of a genetic construct comprising an ABC1 promoter, such as that disclosed in Figure 3 (BAC RPCI-11 317 for human ABC1, recited in amended claim 194), operably linked to a reporter gene, as supported in the application, especially at page 8, lines 17-28, in combination with the genomic structure shown in Figure 3.

It is noted in the Office Action that at the time of filing of the present application, a physiological role for ABC1 had not been established (at page 9 of the Office Action, citing Luciani et al (EMBO J 15:226-235 at column 2, end of the first paragraph). Applicants note that Figures 1 and 2 serve to establish such a role by linking ABC1 gene transmission and mutation with HDL-C levels in the individuals depicted and reiterate the above-referenced justification for this. Thus, Applicants for the first time herein teach a physiological function for ABC1.

Rejection Under 35 U.S.C. §102

Claims 139 and 141 were rejected under section 102(b) as anticipated by Luciani et al (1996), which teaches use of an antibody to negative binding of ATP. These claims have been cancelled.

Claims 161-163 and 165 were rejected under section 102(b) as being anticipated by Becq et al, which teaches use of human ABC1 expressed in Xenopus laevis cells for anion transport and a number of inhibitors of the same.

Applicant responds that claim 161, and thus claims dependent therefrom, has been amended to recite use of a human ABC1 containing amino acid residues 1-60 of SEQ ID NO: 1 and claim 165 has been amended to recite a human ABC1 containing the sequence of SEQ ID NO: 1. The Becq reference does not teach use of these sequencec.

Claims 161, 164, and 166-168 were rejected under section 102(b) as anticipated by the Hamon reference, which shows anion efflux from mouse macrophages in the presence of zero or increasing concentrations of ABC1 inhibitors and a method for

measuring relative percentage secretion of interleukin 1 from mouse macrophages and human monocytes in the presence of increasing concentrations of inhibitors.

Applicant responds that, in view of the amendment to claim 161 already described, the Hamon reference does not anticipate claim 161 (or claims dependent therefrom). Claim 164 has been cancelled. Claim 166 has been amended in a way similar to 161 and claim 168 amended to recite a protein comprising the sequence of SEQ ID NO: 1. Thus, Hamon does not anticipate the claims as amended.

In response, Applicants have amended claim 161, and claims dependent therefrom, to recite use of a human ABC1 protein comprising amino acid residues 1-60 of SEQ ID NO: 1.

Claim 166, and claims dependent therefrom, directed to use of an assay involving interleukin binding, has been amended to require that the compound found to be a modulating agent be useful in treating a coronary artery disease. This is fully enabled because Applicants for the first time teach the involvement of ABC1 in the occurrence of coronary artery disease within human families.

Rejection Under 35 U.S.C. §102/103

Claim 135 and 137 were rejected under section 102 and/or 103 based on the Luciani et al (1996). This reference describes use of antibodies to bind to mouse ABC1 and the rejection urges that a showing of an antibody that binds to ABC1 ATP binding domain is a showing of an ABC1 modulating agent because it would prevent ATP binding and thus ATP hydrolysis as well. Applicant notes that there is more than one Luciaini reference in the record and Applicant assumes that this reference (and not the Luciani et al (1994) reference) is being relied on by the Examiner.

In response, Applicant has amended claim 135 to recite use of human ABC1 rather than the mouse ABC1 of Luciani et al. In addition, claim 137 has been cancelled. Applicant also notes that the Luciani et al (1996) reference teaches use of polyclonal antibodies raised against a short segment of ABC1 to block macrophage engulfment. There is no measurement of ATP binding. Conversely, Applicants teach measuring a difference in ATP binding (or hydrolysis) using human ABC1 in amended claim 135. In addition, Applicant reiterates that those in the art would have no motivation to look for modulators of ABC1 because a physiological function had not yet been established at the time the application was filed.

Claims 136 and 140 were rejected under section 102 and/or 103 based on the Becq reference as teaching a way of determining increase in ABC1 activity. In response, claim 140 has been cancelled and claim 136, which depends from amended claim 135, also recites all of the same limitations.

Rejection Under 35 U.S.C. §103

Claims138 and 142 were rejected under section 103(a) as being unpatentable over Luciani (Applicant assumes this means the 1996 reference).

In response, claim 138 has been amended to recite use of a human ABC1 comprising amino acids 1-60 of SEQ ID NO: 1. Claim 142 has been amended to recite use of a human ABC1 protein comprising the amino acid sequence of SEQ ID NO: 1. Use of such a protein could not have been obvious because, even if it were obvious to extend the mouse results of Luciani to the corresponding human protein, it was not known prior to Applicants' teaching that human ABC1 comprised this sequence. In addition, there would be no motivation to do so because the physiological role of ABC1

was unknown at the time the application was filed (as Luciani admits). In addition, unlike the application, Luciani does not teach any assays for modulating activity and does not measure either ATP binding or hydrolysis.

Claim 164 was rejected under section 103(a) as unpatentable over Becq. In response, Applicant has cancelled claim 164.

Claim 165 was rejected under section 103(a) as unpatentable over Hamon. In response, claim 165 has been amended to recite use of a human ABC1 having the amino acid sequence of SEQ ID NO: 1 where the compounds are useful in modulating plasma cholesterol levels. Hamon does not suggest any amino acid sequence although he does use human monocytes for these studies, which might make use of such sequence inherent. However, Hamon provides no motivation to find modulators of ABC1 because no physiological function was known prior to the teaching of the present application that ABC1 is involved in regulating plasma cholesterol levels, such as triglyceride, cholesterol and HDL-cholesterol.

Claims 169-171 were rejected under section 103(b) as unpatentable over Becq in view of Hamon.

In response, Applicants have cancelled claims 170 and 171. Claim 169 has been amended to recite use of a human ABC1 comprising the first 60 amino acids of SEQ ID NO: 1 a specific sequence and wherein the compound is useful for modulating plasma cholesterol levels in a mammal. Hamon would provide no motivation to do this because Applicants were the first to teach this role for ABC1.

Claim 172 was rejected under section 103(a) as unpatentable over Becq in view of Hamon. In response, claim 172 has been amended to delete the reference to casein kinase and instead to recite the limitations of claim 169 along with use of an intact cell.

Claims 189, 190, and 192-194 were rejected under section 103(a) as unpatentable over Hamon in view of GenBank Accession No. AJ012376. In response, claim 189, and all claims dependent therefrom, has been amended to recite use of a genetic construct comprising an ABC1 promoter, such as that disclosed in Figure 3 (BAC RPCI-11 317 for human ABC1, recited in amended claim 194), operably linked to a reporter gene, as supported in the application, especially at page 8, lines 17-28, in combination with the genomic structure shown in Figure 3. The full sequence for the region incorporating the promoter is contained in priority U.S. provisional application 60/151,977, filed September 1, 1999, on which the present application relies in part.

In addition, the nucleotide sequence of GenBank Accession No. AJ012376 is incorrect and/or incomplete, as disclosed by Applicants (see the application at page 38, lines 7-19, and page 40, line 17, to page 41, line 5). For example, it does not contain residues 1-60.

New Claims

Applicant has added new claims 197 - 212, which are intended to better describe the invention.

Claims 197-201 are directed to a process for identifying a cholesterol level modulating agent by testing compounds found to be ABC1 modulating agents using the process of claim 135 (which assays ATP binding or hydrolysis). Support for these claims is found in the application, especially at page 72, line 15, to page 73, line 7.

Claims 202-205 are directed to a process for identifying a triglyceride level modulating agent by testing compounds found to be ABC1 modulating agents using the process of claim 143 (which measures effects on lipid transport across a membrane). Support for these claims is found in the application, especially at page 38, line 24, to

page 39, line 17, and at page 55, lines 4-17, as well as support already cited for amended claim 143.

Claims 206-210 are directed to a process for identifying a cholesterol level modulating agent by testing compounds found to be ABC1 modulating agents using the process of claim 189 (which measures effects on gene expression). Support for these claims is found in the application, especially at page 72, line 15, to page 73, line 7, and the support for amended claim 189 already cited.

Claim 211 (similar to claim 143) is directed to an assay for modulation of lipid transport by ABC1 from WHAM chicken. Claim support is found in the application, especially at page 23, lines 6-10, at page 72-lines 6-8, and at page 73, line 22 to page 76, line 3. Claim 212 (similar to claim 143) is directed to an assay for modulation of lipid transport by ABC1 from C. elegans. Claim support is found in the application, especially at page 19, lines 6-9, at page 20, line 5 and line 24, page 37, lines 19-21, at page 41, lines 15-21 and at page 58, line 25, to page 59, line 2.

Applicant has enclosed herewith a Request for a 1 month extension of time to respond to the Office Action, along with the fee for a large entity.

The Commissioner is requested to charge any additional fees, or credit any refunds, to Deposit Acc't No. 03-0678.

EXPRESS MAIL CERTIFICATE

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Deposit Date: 11 September 2002

I hereby certify that this paper and the attachments hereto are being deposited today with the U.S. Postal Service "Express Mail Post Office To Addressee" service under 37 CFR 1.10 on the date indicated above addressed to:

Commissioner for Patents
Washington, DC 20231

Alan J. Grant 9/11/02
Alan J. Grant, Esq. **Date**

Respectfully submitted,

Alan J. Grant

Alan J. Grant, Esq.
Reg. No. 33,389
CARELLA, BYRNE, BAIN, GILFILLAN,
CECCHI, STEWART & OLSTEIN
6 Becker Farm Road
Roseland, NJ 07068
Tel. No.: (973) 994-1700

AMENDED CLAIMS

135. (Amended) A process for identifying a compound that modulates mammalian ABC1 (ABC1) polypeptide biological activity comprising contacting a compound with a ~~mammalian~~ human ABC1 polypeptide that has ABC1 biological activity and in the presence of adenosine triphosphate (ATP) under conditions promoting ~~hydrolysis of ATP by~~ the biological activity of said ABC1 polypeptide and detecting a difference in said ~~hydrolysis~~ biological activity following said contacting relative to when said compound is not present thereby identifying ~~a~~ an ABC1 modulating agent, wherein said biological activity is binding or hydolysis of adenosine triphosphate (ATP).

136. (Amended) The process of claim 135 wherein said difference in ~~hydrolysis~~ biological activity is an increase in ~~the rate of hydrolysis~~ biological activity.

138. The process of claim 135 wherein said ~~mammalian ABC1 is~~ human ABC1 (hABC1) comprises amino acids 1-60 of SEQ ID NO: 1

142. The process of claim ~~139~~ 135 wherein said ~~mammalian ABC1 is~~ human ABC1 (hABC1) comprises the amino acid sequence of SEQ ID NO: 1

143. (Twice Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity comprising contacting a compound with a membrane comprising a mammalian ABC1 polypeptide, in the presence of a lipid under conditions promoting transport of said lipid across said membrane, wherein said lipid is phospholipid or cholesterol, and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

144. (Amended) The process of claim 143 further comprising contact with an acceptor that accepts the transported lipid, said acceptor being a member selected from the group consisting of phospholipid, high density lipoprotein (HDL), Apolipoprotein (Apo) AI, ApoAII and ApoE.

145. (Amended) The process of claim ~~144~~ 143 wherein said ~~acceptor is an HDL particle~~ compound is useful in treating coronary artery disease (CAD).

149. The process of claim 148 wherein said cell is a fibroblast or a macrophage.

158. (Amended) The process of claim ~~144 — 156~~ 143 wherein said mammalian ABC1 is human ABC1.

159. (Amended) The process of claim ~~143~~ 158 wherein said ~~mammalian ABC1 is~~ human ABC1 comprises amino acid residues 1-60 of SEQ ID NO: 1.

160. (Amended) The process of claim ~~144 — 156~~ 158 wherein said ~~mammalian ABC1 is~~ human ABC1 comprises the amino acid sequence of SEQ ID NO: 1.

161. (Twice Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity and is useful in modulating plasma cholesterol levels in a mammal comprising contacting a compound with a membrane comprising a ~~mammalian~~ human ABC1 polypeptide, wherein said polypeptide comprises amino acid residues 1-60 of SEQ ID NO: 1, and a source of one or more anions under conditions promoting transport of said one or more anions across said membrane and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

162. (Amended) The process of claim ~~160~~ 161 wherein said difference in anion transport is an increase in said transport.

163. (Amended) The process of claim ~~160~~ 161 wherein when said one or more anions comprises at least two different anions.

165. (Twice Amended) The process of claim ~~160~~ 161 wherein said ~~mammalian ABC1 is~~ human ABC1 comprises the amino acid sequence of SEQ ID NO: 1.

166. (Amended) A process for identifying a compound that modulates mammalian ABC1 polypeptide biological activity for use in treating CAD comprising contacting a compound with a membrane comprising a ~~mammalian~~ human ABC1 polypeptide and interleukin-1 under conditions promoting transport of said interleukin-1 across said membrane and detecting a difference in said transport following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent useful for treating CAD.

167. (Amended) The process of claim 166 wherein said ~~mammalian ABC1 is mouse ABC1~~ human ABC1 comprises amino acids 1-60 of SEQ ID NO: 1.

168. The process of claim ~~166~~ 167 wherein said ~~mammalian ABC1 is~~ human ABC1 comprises the amino acid sequence of SEQ ID NO: 1.

169. (Amended) A process for identifying a compound that modulates mammalian ABC1 ~~polypeptide~~ protein biological activity and is useful in modulating human plasma cholesterol levels comprising contacting a compound with a ~~mammalian~~ human ABC1 ~~polypeptide~~ protein that has ABC1 biological activity and in the presence of a protein that binds to ~~mammalian~~ said human ABC1 ~~polypeptides~~ protein under conditions promoting binding of said protein to said ABC1 polypeptide, wherein said human ABC1 protein comprises amino acids 1-60 of SEQ ID NO: 1, and detecting a

difference in said binding following said contacting relative to when said compound is not present thereby identifying a mammalian ABC1 modulating agent.

172. (Amended) The process of claim ~~169 wherein said protein is casein kinase~~ membrane is part of an intact cell.

173. (Amended) The process of claim ~~161-172~~ 172 wherein said ~~membrane is part of an intact~~ cell is a recombinant cell.

174. (Amended) The process of claim ~~120, 133, 134, 138, 142, 159, 160, 165, 168 or 171~~ 161 wherein said ~~human ABC1 polypeptide comprises amino acid residues 1-60 of SEQ ID NO: 1~~ membrane is part of an intact cell.

175. (Amended) The process of claim ~~120, 133, 134, 138, 142, 159, 160, 165, 168 or 171~~ 166 wherein said ~~human ABC1 polypeptide comprises the amino acid residues of SEQ ID NO: 1~~ membrane is part of an intact cell.

176. (Amended) A process for identifying a compound that modulates mutant human ABC1 (hABC1) polypeptide biological activity comprising contacting a compound with a mutant hABC1 polypeptide, comprising from 1 to 5 amino acid differences relative to the sequence of SEQ ID NO: 1, and a member selected from the group consisting of a lipid, a protein, ATP, and interleukin-1, and detecting a difference in said biological activity following said contacting relative to when said compound is not present thereby identifying a mutant hABC1 modulating agent.

179. (Amended) The process of claim ~~112-178~~ 143 wherein said hABC1 comprises a detectable label.

181. (Amended) The process of claims ~~112-180~~ 143 wherein said ABC1 polypeptide is a recombinant polypeptide.

184. (Amended) A process for identifying a compound that modulates cholesterol levels in ~~an animal~~ a mammal comprising administering to ~~an animal~~ said mammal an effective amount of a compound ~~identified as a modulator of ABC1 activity using an assay of claims 112 to 181~~ that has ABC1 modulating activity in the process of claim 143 and determining a difference in cholesterol level in said ~~animal~~ mammal following said ~~administration~~ thereby identifying a compound that modulates cholesterol levels in a mammal.

188. (Amended) The process of claim ~~187~~ 182 wherein said mammal is a human.

189. (Amended) A process for identifying a compound that modulates ~~human~~ ABC1 ~~(hABC1)~~ ~~polypeptide biological activity~~ expression comprising contacting a compound with a cell that expresses a ~~hABC1 polypeptide~~ polynucleotide construct, said construct comprising a mammalian ABC1 promoter operably linked to a reporter gene, under conditions promoting ~~said~~ expression of said reporter gene and detecting a difference in said expression in the presence of said compound relative to when said compound is not present, wherein said expression is synthesis of mRNA or protein, thereby identifying a compound that modulates ~~hABC1 biological activity~~ ABC1 expression.

193. (Amended) The process of claim 189 wherein said cell is a fibroblast or a macrophage.

194. (Amended) The process of claim 189 wherein said ~~cell is a macrophage~~ promoter is the promoter found in BAC RPCI -11 317.